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Process for preparing polyvinylpyrrolidone-iodine in aqueous solution

- 5 The present invention relates to a process for preparing polyvinylpyrrolidone-iodine (PVP-iodine) in aqueous solution. Polyvinylpyrrolidone-iodine is the product of the reaction of polyvinylpyrrolidone (PVP) with elemental iodine, which is increasingly used because of its germicidal, bactericidal, 10 fungicidal and disinfectant properties.

Processes for preparing PVP-iodine are known in principle. Preparation ordinarily takes place by mixing polyvinylpyrrolidone as solid or solution with iodine or iodine compounds. However, 15 problems arise in the preparation of PVP-iodine with good stability together with good availability of the iodine content.

- One measure of the stability of a PVP-iodine is the distribution coefficient (DC) of the iodine between an aqueous PVP-iodine 20 solution and heptane. This is determined according to US-A-3,028,300 by vigorously shaking an iodine solution with an available iodine content of 1.0% with heptane at 25°C for one minute and is, if the binding between polyvinylpyrrolidone and iodine is sufficiently strong, about 200 or above. Another 25 measure of the stability, in particular the storage stability, of PVP-iodine is determination of the iodine loss, i.e. the percentage decrease in available iodine, on heating for a defined period.
- 30 An important characteristic variable for the stability of PVP-iodine is the iodine:iodide ratio. When the iodine:iodide ratio is about 2:1 the linkage of PVP and iodine is ordinarily so strong that an iodine odor is no longer perceptible and a moist potassium iodide/starch paper introduced into the gas space above 35 the sample does not develop a color.

- A number of publications, e.g. DE-B 10 37 075, US-A 2,900,305, US-A 2,826,532, US-A 3,028,300, US-A 3,898,326 and DE-B 24 39 197, describe procedures intended to provide 40 PVP-iodine with improved properties. However, the aforementioned processes either lead to PVP-iodine complexes with unsatisfactory stability or require for the formation of a sufficiently strong binding between PVP and iodine a heat treatment, i.e. the PVP-iodine which has been formed is subsequently heated at 45 temperatures of from 70 to 90°C ordinarily for a period of more than 10 hours, in most cases in the range from 20 to 64 hours. To achieve acceptable preparation times, the heat treatment must be

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carried out at comparatively high temperatures, i.e. above 70°C. The heat treatment of PVP-iodine in powder form is technically very elaborate because the powder is very prone to aggregation at these temperatures. If, on the other hand, the heat treatment is
5 carried out in aqueous solution, there is usually observed to be a large loss of iodine through formation of a sediment and/or through sublimation at the necessary temperatures.

DE-A 25 40 170 describes the use of a polyvinylpyrrolidone and
10 alkali metal iodides as iodine ion-providing compound, which lead to PVP-iodine of satisfactory stability without long heat treatment. The resulting PVP-iodine solutions cannot, however, be used for pharmaceutical products because of their ash content.

15 EP-A 027 613 describes a process for preparing PVP-iodine in which PVP, elemental iodine and a compound promoting iodide formation are reacted in aqueous solution. The complete reaction time, i.e. the time referred to as reaction time and the time
20 required for the heat treatment, is in the range from 7 to 32 hours, despite the use of the compound promoting iodide formation, and the complete reaction time required in this process to achieve an iodine loss of less than about 7% is at least 14 hours. The PVP solutions employed are those with a concentration of 50% by weight and a K value of 13, a
25 concentration of 40% by weight and a K value of 17 and a concentration of 30% by weight and a K value of 32.

It is an object of the present invention to provide a process which makes it possible easily and quickly to prepare PVP-iodine
30 starting from elemental iodine. It is additionally intended to provide PVP-iodine which has an improved stability, in particular improved storage stability.

We have found that this object is achieved by a process in which
35 there is conversion of the polyvinylpyrrolidone in aqueous solution with a high concentration and, preferably, a high K value using elemental iodine into polyvinylpyrrolidone-iodine. It was surprising in this connection that on use of polyvinylpyrrolidone solutions in the concentrations of the
40 invention the reaction times are markedly shortened and the PVP-iodine which is formed shows a markedly reduced iodine loss. It was particularly surprising that the PVP solutions and PVP-iodine solutions even with high concentrations and high K values show a comparatively low viscosity and no or only slight
45 increases in viscosity during the process, so that it is ensured that the process is easy to carry out.

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The present invention therefore relates to a process for preparing polyvinylpyrrolidone-iodine in aqueous solution, where an aqueous polyvinylpyrrolidone solution and at least 4.0% by weight of elemental iodine, based on the polyvinylpyrrolidone
5 calculated as solid, are mixed, wherein at the time of mixing the concentration c of the aqueous polyvinylpyrrolidone, based on the total amount of polyvinylpyrrolidone and water, and the K value of polyvinylpyrrolidone obeys the following relation:

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$$c > 100 \times [0.1 + 8 : (K + 5)]$$

where c is stated in % by weight, and the Fikentscher K value is in the range from 10 to 100. The concentration c therefore relates only to the ratio of polyvinylpyrrolidone to water.

15 The polyvinylpyrrolidone-iodine solutions prepared by the process of the invention, and the solid PVP-iodine obtainable therefrom by removing the water and other volatile constituents, preferably have an iodine:iodide ratio of about 2:1 and a distribution
20 coefficient (DC), determined as disclosed in US-A 3,028,300, in the range from 190 to 250. The PVP-iodine obtainable according to the invention preferably has an iodine loss of < 6%, preferably < 5% and particularly preferably < 4%, determined on aqueous solutions with an available iodine content of 1.0% after storage
25 at 80°C for 15 hours.

The concentration c in the relation stated above represents a minimum concentration, which depends on the K value of polyvinylpyrrolidone employed, of the solutions to be used
30 according to the invention. It is preferred for the maximum concentration c of the polyvinylpyrrolidone solution during the process of the invention to be below 90% by weight, preferably below 85% by weight and particularly preferably below 80% by weight.

35 The concentration c of the aqueous polyvinylpyrrolidone, based on the total amount of polyvinylpyrrolidone and water, and the K value of the polyvinylpyrrolidone at the time of mixing preferably obeys the relation $c > 100 \times [0.1 + 8 : (K + 2)]$.

40 The Fikentscher K value is a measure of the molecular weight of the polyvinylpyrrolidone and is determined as described by H. Fikentscher, Cellulose-Chemie, 13, 58-64 and 71-74 (1932) as 1% by weight solution in water.

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Polyvinylpyrrolidones suitable for the process of the invention have K values in the range from 10 to 100, preferably 20 to 50 and particularly preferably 25 to 50, e.g. about 30 or about 40. However, it is also possible and advantageous for

- 5 polyvinylpyrrolidones with higher K values to be processed, e.g. polyvinylpyrrolidones with K values of about 70 or about 85, in the process of the invention.

- Polyvinylpyrrolidones with K values in the range from 10 to 20
10 are preferably employed in a concentration c in the range from 65 to 90% by weight, particularly preferably 70 to 85% by weight, in the process of the invention. Polyvinylpyrrolidones with K values in the range from > 20 to 27 are preferably employed in a concentration c of from 43 to 80% by weight, particularly
15 preferably 45 to 70% by weight, in the process of the invention. It is preferred to employ in the process of the invention a polyvinylpyrrolidone solution of a polyvinylpyrrolidone with a K value of > 27 and a polyvinylpyrrolidone content of > 35% by weight. Polyvinylpyrrolidones with a K value in the range from 28
20 to 50, e.g. about 30 or about 40, are preferably employed in a concentration c of 36 to 75% by weight, particularly preferably 42 to 65% by weight and very particularly preferably 45 to 55% by weight, e.g. about 45% by weight. Polyvinylpyrrolidones with a K value in the range from > 50 to 100, e.g. about 60, about 70 or
25 about 90, are preferably employed in a concentration c of from 18 to 50% by weight, particularly preferably 19 to 40% by weight and very particularly preferably 20 to 35% by weight, e.g. about 25% by weight.

- 30 The polyvinylpyrrolidone employed in the process of the invention can in principle be obtained in any way. Polyvinylpyrrolidone suitable for the process of the invention can be prepared, for example, by polymerization in an organic solvent such as isopropanol or toluene, using free-radical formers, especially
35 organic peroxy compounds, e.g. dialkyl peroxides, or azo compounds, e.g. AIBN, and subsequently be subjected where appropriate to an after-treatment, e.g. a steam distillation. The polyvinylpyrrolidone can, for example, also be prepared by free-radical polymerization in water, where appropriate mixed
40 with organic solvents in the presence of water-soluble free-radical formers, e.g. hydrogen peroxide or sodium peroxodisulfate. A number of process for preparing polyvinylpyrrolidone are known to the skilled worker and are described, for example in Houben-Weyl, Methoden der Organischen
45 Chemie, Georg Thieme-Verlag, Stuttgart.

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- Also suitable for the process of the invention are polyvinylpyrrolidones subjected to a hydrogenation process after the polymerization. This involves hydrogenation of the polyvinylpyrrolidone by conventional known processes. A
- 5 hydrogenation with hydrogen is described, for example, in US-A 2,914,516. Likewise suitable are polyvinylpyrrolidones which have been treated with complex hydrides, which are described, for example, in EP-A 027 613.
- 10 The polyvinylpyrrolidones described in DE-B 28 18 767, EP-A 027 613, the processes for preparing them and suitable reactants and reaction conditions can also be employed analogously for preparing the highly concentrated polyvinylpyrrolidone solution employed according to the
- 15 invention. Express reference is hereby made to these two publications.

- Further sources of iodine which can be employed besides elemental iodine are iodines or other iodine-providing compounds,
- 20 employing, based on the polyvinylpyrrolidone calculated as solid, at least 4.0% by weight, in particular at least 6.0% by weight and particularly preferably at least 8.0% by weight, of elemental iodine. The elemental iodine will ordinarily be employed in an amount in the range from 5 to 35% by weight, preferably 10 to 30%
- 25 by weight and in particular 15 to 25% by weight, e.g. about 20% by weight. Examples of compounds suitable as further sources of iodine are hydrogen iodide, alkali metal and alkaline earth metal iodides, especially alkali metal iodides, e.g. sodium iodide and potassium iodide, polyiodides, in particular alkali metal
- 30 polyiodides, ammonium iodides, in particular tetraalkylammonium iodides, e.g. tetramethylammonium iodide, phosphorus triiodide, and organic acid iodides, e.g. acetyl iodide. It is preferred for at least 50%, in particular at least 75% and particularly preferably at least 90%, of the iodine present in the
- 35 polyvinylpyrrolidone-iodine to be employed in the form of elemental iodine. In a preferred embodiment of the process of the invention, elemental iodine is employed as the exclusive source of iodine.
- 40 In the process of the invention it is possible for the reactants, i.e. iodine, polyvinylpyrrolidone and, where appropriate, reducing agent and, where appropriate, auxiliaries to be mixed, independently of one another, undiluted or in suspension or solution. The mixing of the reactants to form the PVP-iodine is
- 45 carried out at a concentration c as defined above.

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- It is possible, for example, in the process of the invention for the iodine and, where appropriate, further sources of iodine to be introduced into a solvent, preferably water, and be heated where appropriate. Subsequently, the polyvinylpyrrolidone, 5 preferably as aqueous solution, is added and the reaction mixture is mixed. The mixing of the reactants can take place at the same temperature as the addition of the polyvinylpyrrolidone or at another, preferably a higher, temperature.
- 10 In the process of the invention, preferably the polyvinylpyrrolidone is introduced as aqueous solution and heated where appropriate. Subsequently, iodine and, where appropriate, further sources of iodine are added, and the reaction mixture is mixed. The addition of the iodine and, where appropriate, the further 15 sources of iodine can take place all at once, in a plurality of portions or continuously. The mixing can take place at the same temperature as the addition of the iodine and, where appropriate, of the further sources of iodine or at another, preferably a higher, temperature.
- 20 The iodine and, where appropriate, the further sources of iodine can be added undiluted or as suspension or solution, e.g. in water or organic solvents.
- 25 It is preferred for at least the mixing of the reactants, in particular the polyvinylpyrrolidone and the iodine, to be carried out at a temperature above 50°C.
- When the process of the invention is carried out in the presence 30 of a reducing agent, the addition can take place in whole or in part by premixing the reducing agent and PVP and/or by adding reducing agent to the initial charge and/or by adding reducing agent during the mixing.
- 35 For the purposes of this invention, mixing means a blending or homogenization intended to increase the contact of the components to be mixed, also referred to as reactants herein, and thus make a uniform and/or rapid formation of the desired product possible. It is possible by the mixing to generate a mixture which is as 40 homogeneous as possible and/or to initiate or speed up a chemical reaction.
- Methods capable of bringing about mixing are, for example, stirring, shaking, injection of gases or liquids and exposure to 45 ultrasound.

Suitable processes and devices bringing about mixing are known to the skilled worker. Examples of suitable mixing devices are those also employed for mixing in plastics technology. Suitable devices are described, for example, in "Mischen beim Herstellen und
5 Verarbeiten von Kunststoffen", H. Pahl, VDI-Verlag 1986. Suitable mixing apparatuses are, for example, stirred vessels, dynamic and static mixers, single-shaft stirrers, for example stirrers with stripper mechanisms, especially paste mixers, multishaft stirrers especially PDSM mixers, solids mixers, and mixer/kneader reactors
10 (e.g. ORP, CRP, AP, DTP from List and Reaktotherm from Krauss-Maffei), x trough mixers and internal mixers, extruders, e.g. the ZKS models from Werner & Pfleiderer, and rotor-stator systems, e.g. Dispax from Ika. Suitable extruders are, for example, single-screw machines, intermeshing screw machines or
15 else multiscrew extruders, especially twin screw extruders, e.g. corotating or counterrotating twin screw extruders. Heatable mixing devices are preferably used.

The process of the invention is preferably carried out at a
20 temperature in the range from 10 to 110°C, preferably in the range from 20 to 105°C. It is preferred for the reaction time in the process of the invention to be from 20 minutes to 20 hours, preferably 30 minutes to 12 hours and particularly preferably 1 hour to 6.5 hours. Within the meaning of this invention, the
25 reaction time means the time between the first contact of a source of iodine with polyvinylpyrrolidone in aqueous solution until a stable PVP-iodine solution is present. A stable PVP-iodine solution means for the purposes of this invention preferably a PVP-iodine solution which shows an iodine loss
30 within the aforementioned limits determined by the aforementioned methods.

In the process of the invention it is preferred that the mixture is heated at a temperature in the range from 50 to 110°C, in
35 particular 70 to 105°C and very particularly preferably in the range from 85 to 100°C for a period of from 30 minutes to 15 hours, in particular 60 minutes to 12 hours and particularly preferably 60 minutes to 6.5 hours.

40 The mixing can also be carried out in the presence of a reducing agent. Suitable reducing agents are, in particular, those able to promote the formation of iodide from elemental iodine. Particularly suitable compounds are those which after the reaction with iodine form exclusively volatile substances such
45 as, for example, carbon dioxide or nitrogen in addition to the iodide and, where appropriate, water. The reducing agent is preferably selected from formic acid, oxalic acid, the esters and

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salts of formic and oxalic acids, and the amides of carbonic acid, of formic acid and of oxalic acid.

Examples of particularly suitable reducing agents are ammonium
5 carbonate, ammonium bicarbonate, ammonium carbamate, urea, ammonium formate, formamide, ammonium oxalate, oxamic acid and oxamide. Oxalic acid and formic acid, and their amides and ammonium salts, are particularly preferred. Oxalic acid and formic acid are very particularly preferred and, in the reaction
10 with iodine, form only carbon dioxide in addition to hydrogen iodide.

The amount of reducing agent is ordinarily such that, when reaction is complete, $1/5$ to $2/5$, preferably about $1/3$, of the
15 added iodine is converted into iodide. The amount is therefore between 2 and 30% by weight, preferably 4 and 22% by weight, calculated according to the iodine employed, depending on the nature of the addition.

20 It is preferred for the polyvinylpyrrolidone-iodine solutions prepared by the process of the invention to have an available iodine content, i.e. iodine which can be titrated with thiosulfate, in the range from 2 to 40% by weight, preferably 4 to 30% by weight and particularly preferably 7.5 to 15% by
25 weight, based on the total weight of PVP-iodine, calculated as solid. The PVP-iodine solutions obtained with this process can be diluted or concentrated virtually as desired, e.g. as far as solid PVP-iodine.

30 The process of the invention is to be explained in more detail hereinafter by means of some embodiments:

The process of the invention can be carried out, for example, in such a way that iodine and, where appropriate, further sources of
35 iodine are added to water and, where appropriate reducing agent, and subsequently PVP solution is added with stirring. It is preferred for the aqueous iodine-containing reaction mixture after the addition of the iodine or the sources of iodine to be vigorously mixed, e.g. for 10 minutes to 120 minutes, before the
40 PVP solution is added. It is preferred for the reaction mixture to be heated after the addition of the PVP solution to 70 to 100°C, e.g. about 90°C, over the course of 10 minutes to 2 hours, e.g. about 1 hour, and subsequently be mixed further for 2 to 10 hours.

In a preferred embodiment of the process of the invention, the polyvinylpyrrolidone solution and, where appropriate, reducing agent are heated to a temperature in the range from 50 to 110°C, preferably 70 to 105°C and particularly preferably to a
5 temperature of about 85°C or about 100°C, at this temperature elemental iodine and, where appropriate, further sources of iodine are added, and the reactants are mixed for 2 to 12 hours, preferably 2.5 to 10 hours and particularly preferably 3 to
10 6.5 hours. The addition of the elemental iodine and, where appropriate, of the further sources of iodine can take place in one portion, in 2 to 15 portions, for example 5 or 10 portions, or continuously. If the iodine or the sources of iodine are added in a plurality of portions or continuously, the addition preferably takes place over a period of from 20 to 90, preferably
15 30 to 70 and particularly preferably 40 to 60, minutes.

In a particularly preferred embodiment of the process of the invention, a PVP solution of a polyvinylpyrrolidone with a K value of > 27 and a concentration c of about 45% by weight is
20 mixed with a reducing agent, preferably formic acid, and then elemental iodine is added in a plurality of portions, preferably about 10 identical portions, the interval between the individual portions being a few minutes, preferably about 5 to 10 minutes. The iodine can be added in the region of room temperature, e.g.
25 about 25°C, or to the initial charge which has been heated to a temperature in the range from 40 to 100°C, e.g. about 50°C or about 85°C. After the addition is complete, the reaction mixture is mixed at a temperature in the range from 70 to 100°C, e.g. about 85°C, for a further 2 to 6 hours. The reaction mixture can
30 subsequently only be diluted by addition of water, for example to a solids content in the range from 5 to 40% by weight, such as about 20% by weight or about 30% by weight.

The polyvinylpyrrolidone-iodine solutions obtainable by this
35 process preferably have an available iodine content of at least 4% by weight, based on the polyvinylpyrrolidone-iodine, calculated as solid.

The PVP-iodine solutions prepared according to the invention can
40 be formulated directly in a conventional way, e.g. with addition of further auxiliaries, for example surfactants, to the final products intended for the user. These solutions generally have a total solids concentration of from 10 to 50% by weight.

45 The present invention further relates to a polyvinylpyrrolidone-iodine solution obtainable by a process as described above. The PVP-iodine solutions of the invention preferably comprise a

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polyvinylpyrrolidone with a K value of from 25 to 90 and, in particular, 25 to 35 and a PVP-iodine solids content in the range from 25 to 55% by weight, in particular 30 to 50% by weight. The PVP-iodine solutions of the invention advantageously show an
5 iodine loss of less than 4%, determined after 15 h at 80°C, and a free iodine (volatile iodine) content of less than 2 ppm.

The present invention further relates to a solid polyvinylpyrrolidone-iodine obtainable by removing the water and
10 other volatile constituents from an aqueous polyvinylpyrrolidone-iodine solution as defined above.

The present invention further relates to the use of an aqueous polyvinylpyrrolidone-iodine solution or of solid
15 polyvinylpyrrolidone-iodine as defined above for producing compositions for disinfection, antiseptis or for wound treatment, and for producing wound coverings.

The present invention further relates to an antiseptic
20 composition comprising an aqueous polyvinylpyrrolidone-iodine solution or solid polyvinylpyrrolidone-iodine as described above.

A further advantage of the polyvinylpyrrolidone-iodine solution obtainable according to the invention is that it can be employed
25 directly as solution and it is unnecessary first to isolate the PVP-iodine from the aqueous solution since the PVP-iodine solutions prepared according to the invention have advantageously high concentrations. It is therefore not ordinarily necessary for them to undergo elaborate concentration; on the contrary, they
30 can be formulated directly, where appropriate after dilution, to PVP-iodine solutions ready for use. The high concentration of the PVP-iodine solutions prepared according to the invention is also advantageous if the intention is to prepare therefrom, by removing the water and other volatile constituents, solid
35 polyvinylpyrrolidone-iodine, for example polyvinylpyrrolidone-iodine powder or granules, since fewer volatile constituents, in particular water, need to be removed. The novel polyvinylpyrrolidone-iodine solutions obtainable by this process surprisingly have, despite the reduced reaction time, a greater
40 stability than conventional solutions, as is evident in particular from an iodine loss of < 5%.

Solid PVP-iodine can, if desired, be obtained from the PVP-iodine solutions obtained according to the invention for example by
45 precipitating the PVP-iodine from the solution and, where appropriate, subsequently filtering off, or by a drying process,

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for example by freeze-drying, drum drying, spray drying or spray granulation.

The following examples illustrate the invention without
5 restricting it. The K values were determined as described by
H. Fikentscher (see above). The iodine loss (IL) was determined
by storing an aqueous PVP-iodine solution with an available
iodine content of 1% at a temperature of 80°C for 15 hours. The
distribution coefficient (DC) was determined as described in
10 US-A 3,028,300 by vigorously shaking 1.0 ml of an aqueous
PVP-iodine solution with an available iodine content of 1.0% with
25 ml of heptane in a closed glass flask in a thermostated
heating bath at 25°C for 1 minute. After standing for some
minutes, the two phases were separated and the iodine content in
15 the aqueous phase was determined by titration with sodium
thiosulfate and the iodine content in the heptane phase was
determined by spectrophotometry. The calculation took place in
accordance with the following equation:

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$$DC = \frac{\text{mg of iodine in H}_2\text{O phase}}{\text{mg of iodine in heptane}} \times \frac{\text{ml of heptane (25)}}{\text{ml H}_2\text{O phase (1)}}$$

25 Examples

The analytical data of the comparative example (CE1) and the
examples according to the invention (E2 to E9) are compiled in
table 1.

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Comparative example 1

1 140 g of a 17.5% by weight polyvinylpyrrolidone solution of a
polyvinylpyrrolidone with a K value of 30 and 1.86 g of formic
35 acid were introduced into a stirred reactor. Then, while
stirring, 35 g of elemental iodine were added in 10 equal
portions at intervals of about 5 minutes. The reaction mixture
was then heated to 70°C while stirring and stirred at this
temperature for a further 20 hours. The reaction mixture had an
40 inconsistent viscosity because of agglomerates.

Example 2

733 g of polyvinylpyrrolidone solution of a polyvinylpyrrolidone
45 with a K value of 30 and a concentration c of 45% by weight and
3.72 g of formic acid were introduced into a stirred vessel and
heated to 100°C. Then, while stirring, 70 g of elemental iodine

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were added in 10 equal portions at intervals of about 5 minutes. This was followed by stirring at this temperature for a further 10 hours. The reaction mixture was then diluted with water to a solids content of 30.0% by weight.

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Example 3

1.369 kg of polyvinylpyrrolidone solution of a polyvinylpyrrolidone with a K value of 30 and a concentration c of 45% by weight and 6.95 g of formic acid were introduced into a stirred vessel and heated to 85°C while stirring. Then, while stirring, 131 g of elemental iodine were added in 10 equal portions at intervals of about 5 minutes. This was followed by stirring the reaction mixture at 85°C for 7.5 hours and then diluting with water to a solids content of 30% by weight.

Example 4

733 g of polyvinylpyrrolidone solution of a polyvinylpyrrolidone with a K value of 30 and a concentration c of 45% by weight and 3.72 g of formic acid were introduced into a stirred vessel and heated to 85°C. Then, while stirring, 70 g of elemental iodine were added in 10 equal portions at intervals of about 5 minutes. This was followed by stirring at this temperature for a further 6 hours. The reaction mixture was then diluted with water to a solids content of 30.0% by weight.

Example 5

Example 5 was carried out in analogy to example 4 in a pilot plant with a scaleup factor of 130.

Example 6

Example 6 was carried out in analogy to example 4, but with stirring at 90°C for 6 hours after completion of the addition of iodine.

Example 7

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733 g of polyvinylpyrrolidone solution of a polyvinylpyrrolidone with a K value of 30 and a concentration c of 45% by weight and 3.72 g of formic acid were introduced into a stirred vessel and heated to 50°C. Then, while stirring, 70 g of elemental iodine were added in 10 equal portions at intervals of about 5 minutes. This was followed by rapidly heating the reaction mixture to 85°C

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while stirring, stirring at 85°C for a further 6 hours and then diluting with water to a solids content of 30% by weight.

Example 8

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Example 8 was carried out in analogy to example 7, but the iodine was added at 25°C, and stirring at 85°C was for only 4 hours.

Example 9

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Example 9 was carried out in analogy to example 8, but stirring at 85°C was for only 3 hours.

No formation of a sediment was observed in any of examples E2 to E9 according to the invention. Examples E2 to E9 according to the invention all had distribution coefficients DC in the region of about 200 or above and met the specifications for use in pharmaceuticals.

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Table 1:

	PVP solution			Red. agent ¹⁾ [g]	Iodine [kg]	Reaction tempera- ture ²⁾ [°C]	Reaction time [hours]	PVP-iodine solution			
	Amount [kg]	C [% by wt]	K value					SC before dilu- tion ³⁾	SC after dilu- tion ³⁾	Avail. iodine ⁴⁾ [% by wt]	Iodine loss ⁵⁾ [% by wt]
CE1	1.140	17.5	30	1.86	0.035	25 / 70	21	19,6	-	9.68	4.38
E2	0.733	45	30	3.72	0.070	100	11	ca. 50	30.0	10.0	4.8
E3	1.369	45	30	6.95	0.131	100	8.5	ca. 50	30.0	10.9	4.6
E4	0.733	45	30	3.72	0.070	85	7	ca. 50	30.0	11.9	1.7
E5 ⁶⁾	178.1	45	30	903	17.03	85	7	ca. 50	29.5	10.8	3.6
E6	0.733	45	30	3.72	0.070	85 / 90	7	ca. 50	30.2	11.4	2.6
E7	0.733	45	30	3.72	0.070	50 / 85	7	ca. 50	29.9	11.6	2.6
E8	0.733	45	30	3.72	0.070	25 / 85	5	ca. 50	29.9	12.25	3.3
E9	0.733	45	30	3.72	0.070	25 / 85	4	ca. 50	30.3	11.86	3.4

1) Formic acid, 100%

2) Where two figures are stated, the first figure relates to the temperature during addition of iodine

3) SC stands for solids content in % by weight

4) Determined by titration with thiosulfate

5) Determined after heating a 1% strength solution at 80°C for 15 hours

6) Pilot plant test